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Original Article

Heart rate variability and cardiorespiratory coupling in obstructive sleep apnea: elderly compared with young

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ABSTRACT

Introduction: Aging is known to be a major contributing factor to the increased risk of obstructive sleep apnea (OSA). With aging, breathing undergoes significant changes during sleep, increasing the prevalence of apnea events, which affects heart rate variability (HRV) and cardiorespiratory coupling (CRC).
Objectives: To compare HRV and CRC during wakefulness and sleep between young and elderly patients with and without OSA; and to determine whether the presence of OSA in young and elderly patients has a different impact on HRV and CRC during sleep.
Methods: One hundred subjects, 50 young (mean age, 27 ± 9; 20 normal and 30 OSA) and 50 elderly (mean age, 65 ± 7; 20 normal and 30 OSA), underwent polysomnography. Spectral, cross-spectrum, and HRV parameters were analyzed during wakefulness and sleep.
Results: The spectral analysis indicated that age affected HRV, with higher values of low frequency ($P < 0.05$) in elderly subjects during wakefulness and an interaction between the presence of OSA and age. OSA influenced HRV during sleep with lower LF/HF ratios during stage 2 (S2) and rapid eye movement (REM) sleep ($P < 0.05$), with an interaction between the presence of OSA and age in REM sleep. Elderly patients had significantly lower percent tachogram power coherent with respiration (%TPCR) during wakefulness ($P < 0.05$), and OSA led to lower %TPCR during S2.
Conclusions: Age and OSA have an unfavorable impact on HRV, with reduced autonomic modulation during wakefulness, S2, and REM sleep. Age affects CRC during wakefulness and the presence of OSA affects CRC during sleep.

1. Introduction

Obstructive sleep apnea (OSA) is a respiratory disorder characterized by recurrent airflow obstruction caused by total or partial collapse of the upper airways [1,2]. Aging is associated with increased apnea prevalence and is thus known to be a major factor contributing to the risk of OSA [3,4]. Moreover, elderly adults with OSA are at greater risk for cardiovascular disease (i.e. coronary artery disease, congestive heart failure, ischemic disease, and stroke) [5,6].

Cardiac autonomic function can be non-invasively assessed by analyzing the heart rate variability (HRV), which quantifies the changes in beat-to-beat intervals influenced by the combined effects of the sympathetic and parasympathetic nervous systems on the heart rate [7]. Clinical studies have consistently reported that decreased HRV is associated with sleep disorders [8–10]. During sleep, HRV is influenced by direct modulation of vagal efferent activity resulting from baroceptor responses to respiratory blood pressure fluctuations and from mechanical sinus node stretch determined by respiration-related changes in venous return [11].

Respiration undergoes important modifications during sleep and HRV is affected by sleep stage organization and by the presence of apnea events [12]. However, it is not known whether the effects of OSA on cardiac autonomic modulation in elderly subjects are different from those in young subjects, both during wakefulness and

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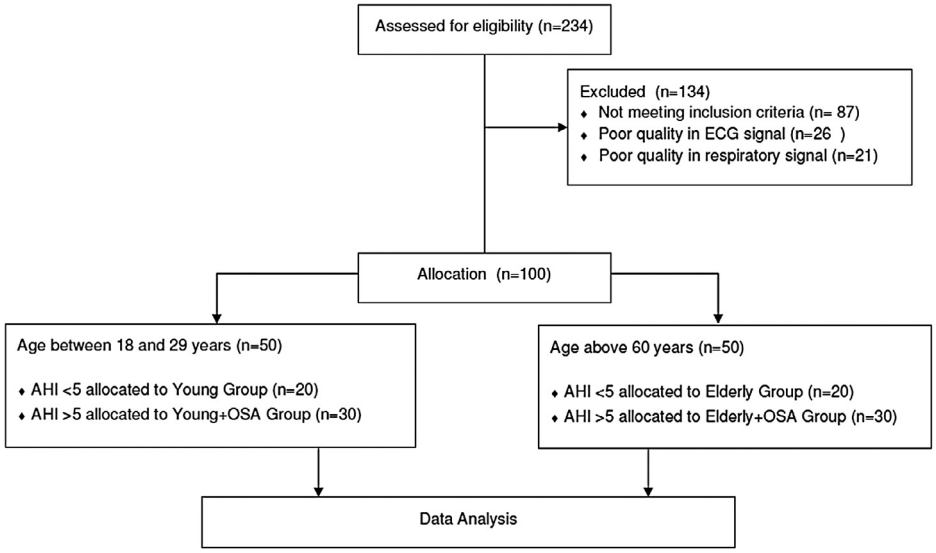

Fig. 1. Experimental protocol. ECG, electrocardiography.

sleep. It is not known whether different effects are likely to be observed during specific sleep stages. Since OSA as it relates to the senescence process is considered a risk factor for cardiac autonomic impairment, we hypothesized that HRV and cardiorespiratory coupling (CRC) would be worse in elderly subjects with OSA.

Therefore, the aim of the study was to contrast HRV and CRC during wakefulness and sleep in young and elderly subjects with OSA. Further, we aimed to determine whether the presence of OSA in young and elderly subjects has a different impact on HRV and CRC during different stages of sleep.

2. Methods

This was a cross-sectional study, by analysis of medical records involving young and elderly patients referred to our sleep medicine clinic between January 2011 and December 2012 for evaluation of excessive daytime somnolence, snoring, and suspected OSA. The study protocol was approved by the Ethics Committee of Federal University of São Carlos (N.401/2010 opinion) and was registered as a clinical trial (RBR-3jbm6d). All participants signed informed consent prior to the polysomnography. The present study was also conducted in full accordance with the Declaration of Helsinki.

2.1. Subjects

The patients completed a questionnaire concerning possible daily or nocturnal symptoms, substance abuse, medication, and medical history. The inclusion criteria in the elderly (aged >60 years) and young (aged 18–29 years) groups were normal electrocardiogram (ECG) during wakefulness and absence of cardiac and respiratory diseases. Exclusion criteria for selection of all subjects were: atrial fibrillation and other cardiac arrhythmias; history of myocardial ischemia, cardiomyopathy or myocardial infarction; cardiac pacemaker; sleep disorders such as periodic limb movement disorder; treatment with antiarrhythmic medications; diabetes and/or uncontrolled hypertension.

Clinically examined elderly patients with an apnea–hypopnea index (AHI) ≥ 5 events/h were assigned to the elderly + OSA group, whereas those with AHI < 5 were assigned to the elderly group. Clinically examined young patients with AHI ≥ 5 were assigned to the young + OSA group and young people with AHI < 5 were assigned to the young group (Fig. 1).

2.2. Signal processing

Nocturnal polysomnography (PSG) recordings were obtained from all subjects using an Icelera Fast-Poli 26i (Homed, São Paulo, Brazil) device and included the monitoring of electroencephalogram, electro-oculogram, oronasal flow by thermistor, transducer nasal pressure, thoracoabdominal movement, ECG, snoring, and body position [13]. A sleep specialist visually scored PSG recordings for sleep stages and apnea events. Total sleep time, number and duration of rapid eye movement (REM) periods, and number and duration of arousals were also measured [14].

Sleep stages, hypopneas, apneas, and arousals were scored using the standard recommended by the American Academy of Sleep Medicine [15,16].

The R peaks were detected on each ECG signal using the Pan–Tompkins algorithm [17]. The respirogram was extracted from each respiration signal by sampling it in correspondence with each R peak identified in the ECG signal [18].

2.3. HRV and CRC analysis

On both the tachogram and the respirogram, segments with 5-min-long portions of the first two complete non-REM (NREM)–REM sleep cycles were carefully checked to avoid arousals, ectopic beats, and artifacts. The more stable segments of sleep stages 2 and 3 and REM sleep were selected. For the wakefulness period, we analyzed a 5 min segment at beginning of the night that was free of ectopic beats and artifacts. Autoregressive (AR) analysis was performed on each tachogram and respiration portion to obtain an AR model to calculate the signal power spectral density, following a method previously described elsewhere [19–21].

In order to analyze the HRV in the frequency domain, spectral components were identified on the HRV signal spectrum in the low frequency (LF, 0.04–0.15 Hz) and in the high frequency (HF, 0.15–0.4 Hz) bands. LF power in normalized units [LF (nu)] and HF power in normalized units [HF (nu)] were also calculated.

The values of the power in the LF and the HF bands and the LF/HF ratio were calculated for each HRV signal portion, whereas only the HF component was considered for the respirogram. A bivariate analysis was conducted on the tachogram and the respirogram portions, in order to obtain the cross-spectrum between them. The coherence between the signals in the HF bands and the

Table 1
Subjects' characteristics: clinical and polysomnographic parameters.

Characteristics	Young ($n = 20$)	Young + OSA ($n = 30$)	Elderly ($n = 20$)	Elderly + OSA ($n = 30$)	*P*		
					Age effect	OSA effect	Interaction
Age (years)	27 ± 6	28 ± 9	65 ± 5	66 ± 5	NA	NA	NA
BMI (kg/m^2)	27 ± 3	37 ± 8	26 ± 3	30 ± 6	0.001	0.001	0.02
AIH (/h)	4 ± 2	31 ± 25	5 ± 6	35 ± 25	0.59	0.001	0.67
Mean saturation (%)	94 ± 1	91 ± 2	92 ± 2	88 ± 6	0.09	0.22	0.54
Nadir saturation (%)	87.0 ± 1	79.5 ± 1	84.4 ± 1	76.2 ± 1	0.059	0.001	0.84
T_{90} (min)	2 ± 3	64 ± 19	44 ± 21	135 ± 17	0.007	0.001	0.45
Arousals (/h)	3 ± 1	16 ± 17	8 ± 5	32 ± 26	0.003	0.001	0.04
ODI (/h)	4 ± 2	30 ± 25	4 ± 3	33 ± 27	0.69	0.001	0.72
Sleep time in S2 (%)	52 ± 5	59 ± 11	56 ± 8	58 ± 9	0.45	0.06	0.22
Sleep time in S3 (%)	25 ± 6	22 ± 8	21 ± 5	22 ± 9	0.11	0.22	0.48
Sleep time in REM (%)	20 ± 6	16 ± 8	18 ± 7	16 ± 7	0.94	0.16	0.33
Sleep efficiency (%)	84 ± 10	85 ± 11	79 ± 11	78 ± 15	0.01	0.94	0.71
Controlled hypertension	0	3 (10%)	6 (30%)	8 (27%)			

OSA, obstructive sleep apnea; NA, not applicable; BMI, body mass index; AHI, apnea hypopnea index; T_{90}, time spent with oxygen saturation <90% (min); ODI, oxygen desaturation index; S2, stage 2; S3, stage 3; REM, rapid eye movement.

percentages of coherent and not-coherent powers between the signals were also calculated. Average values were calculated for each population for LF power, HF power, LF/HF ratio, HF band coherence, percent of tachogram power coherent with respiration (%TPCR), and percent tachogram power not coherent with respiration (%TPNCR) [22].

2.4. Statistical analysis

The distribution of recorded variables was characterized by calculating the mean and standard deviation values. Since some parameters were expected to be non-normally distributed, the median and range were also calculated.

The results were compared using Kruskal–Wallis one-way and two-way analyses of variance on ranks, with post-hoc Dunn's, in order to identify statistically significant differences in: (i) clinical parameters; (ii) tachogram LF and HF power, and LF/HF ratio values; (iii) the respirogram HF power; and (iv) the tachogram–respirogram coherence in the HF band values during wakefulness and different sleep stages. For these analyses, subjects were categorized according to age (young vs elderly) and OSA (OSA vs non-OSA). $P < 0.05$ was considered significant. The analyses were performed with Sigma Plot version 11.0 (Systat Software, Erkrath, Germany).

3. Results

3.1. Sample characteristics

One hundred examinations meeting the inclusion criteria for this study were selected: 50 young subjects (20 young and 30 OSA young) and 50 elderly subjects (20 elderly and 30 OSA elderly) (Table 1). Body mass index (BMI) was influenced by age and OSA, with an interaction between both. As expected, AHI was higher in OSA groups. Nadir saturation was lower in elderly + OSA subjects, and time spent with oxygen saturation <90% (T_{90}) was influenced by both age and OSA ($P < 0.05$). Likewise, the arousal index was influenced by age and OSA, and patients with OSA had higher rates of oxygen desaturation index (ODI) ($P < 0.001$). There were lower values of sleep efficiency in elderly subjects. In young + OSA subjects, 10% presented with controlled hypertension, increasing to 30% and 27% in elderly and elderly + OSA, respectively.

3.2. HRV in young and elderly subjects during different stages of sleep

The main objective of this study was to contrast HRV in young and elderly subjects categorized according to the presence or absence of OSA during wakefulness and different sleep stages. We also sought to determine possible differences between these indices in the four subgroups. First, we compared the HRV parameters, during wakefulness and each sleep stage, to investigate autonomic modulation behavior during each stage in each group.

Figure 2 illustrates different behaviors during transitions between wakefulness and sleep among the four groups. The young group showed a higher LF/HF ratio and LF during REM sleep when compared with wakefulness and S3. We did not observe this behavior in young + OSA, elderly, and elderly + OSA groups ($P > 0.05$).

3.3. Interaction of age and OSA on HRV in young and elderly subjects

Interaction was observed between age and OSA during wakefulness in young and elderly subjects with respect to LF/HF ratio ($P = 0.04$), LF ($P = 0.02$) and HF ($P = 0.02$). During REM sleep we observed interaction between LF/HF ratio, LF, and HF ($P = 0.01$).

When comparing the LF/HF ratio among the four groups during wakefulness and different sleep stages, it was observed that both the young + OSA, elderly, and elderly + OSA subjects had higher values during wakefulness when compared to other groups. During sleep, there were higher LF/HF ratio values during S2 in the young compared with young + OSA, and higher values of LF/HF ratio during REM sleep in young compared with the other groups ($P < 0.05$) (Fig. 3).

When the effect of age on HRV in young and elderly subjects was compared separately, it was observed that age impacted HRV during wakefulness in elderly subjects with higher values of LF and lower HF. When comparing the effect of age on HRV during sleep, elderly subjects presented lower LF/HF ratio and LF values during REM sleep ($P = 0.005$ and $P = 0.003$, respectively; Table 2).

When separately comparing the effect of OSA on HRV in young and elderly subjects, OSA was found to influence HRV in sleep with lower LF/HF ratio and LF values during S2 ($P = 0.012$ and $P = 0.004$, respectively) and during REM sleep ($P = 0.01$ and $P = 0.007$, respectively).

3.4. Cardiorespiratory coupling in young and elderly subjects

The secondary objective of this study was to contrast the CRC of young and elderly subjects in the presence and absence of OSA. To this end, we compared cardiorespiratory synchronization during wakefulness and different sleep stages. Table 3 shows the results of the bivariate analysis, demonstrating coherence between: (i) the tachogram and the respirogram in the HF band; (ii) the %TPCR; and (iii) the %TPNCR during wakefulness and the different sleep stages.

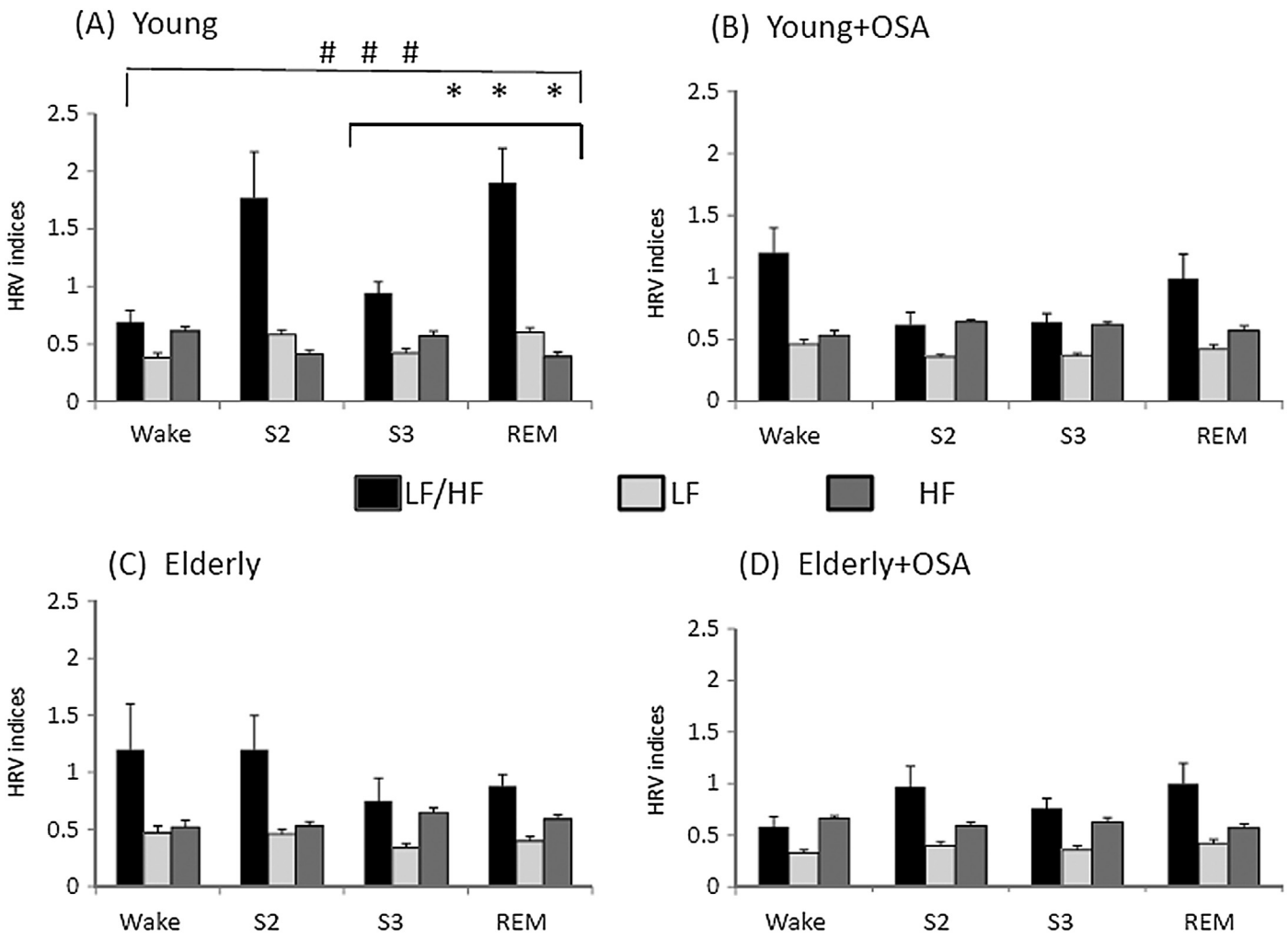

Fig. 2. Heart rate variability (HRV) signal spectrum indices in young and elderly subjects. (A) Young; (B) young + obstructive sleep apnea (OSA); (C) elderly; (D) elderly + OSA. Black bars: low frequency (LF)/high frequency (HF) ratio; light gray bars: LF; dark gray bars: HF. $^{*}P < 0.05$ for difference between stage 3 (S3) and rapid eye movement (REM) sleep. $\#P < 0.05$ for difference between wakefulness and REM sleep.

3.5. Interaction of age and OSA on cardiorespiratory coupling in young and elderly subjects

There were no interactions between age and OSA in cardiorespiratory coupling. When comparing the effects of age on cardiorespiratory synchrony, it was found that young subjects had higher %TPCR during wakefulness compared with elderly subjects ($P = 0.04$); there was no difference during sleep.

When comparing the effects of OSA on cardiorespiratory synchrony, it was observed that OSA groups had lower %TPCR during S2 and lower coherence between the tachogram and the respirogram in the HF band compared with non-OSA subjects ($P = 0.009$ and $P = 0.04$, respectively).

4. Discussion

4.1. Main results

The main results of our study may be summarized as follows: (i) the presence of OSA influenced HRV in young subjects to a greater degree, with a reduction in autonomic modulation during wakefulness and different sleep stages, whereas changes in HRV were only apparent during wakefulness in elderly subjects; (ii) age influenced HRV during wakefulness and sleep in elderly people; (iii) the presence of OSA influenced cardiorespiratory coupling only during wakefulness in both young and elderly subjects; (iv) age influenced HRV in elderly subjects, with a reduction in autonomic modulation during wakefulness and REM sleep; (v) the presence of OSA impacted HRV during sleep, and age and OSA interacted during wakefulness and sleep; (vi) age influenced cardiorespiratory coupling only during wakefulness, and the presence of OSA influenced both young and elderly subjects during sleep.

4.2. HRV during sleep in young and elderly

Self-regulation of the autonomic nervous system decreases with age, and HRV indices are affected by aging [23,24] and OSA severity [9,25]. Few studies have investigated potential damage to the cardiovascular system in OSA in the elderly. Decreased HRV in elderly subjects with OSA may be explained by the fact that reactions of SNA to external stimuli decrease with aging [10,23–28].

Aging is known to be one of the main factors contributing to the risk of OSA, with increasing age associated with increased prevalence. One possible contributing factor to this relationship is the change in body habitus associated with aging – specifically, as the prevalence of obesity increases in the elderly, so too does the risk for OSA [10,23–28]. In the current study, values for BMI were influenced by age and OSA, and there was an interaction between both.

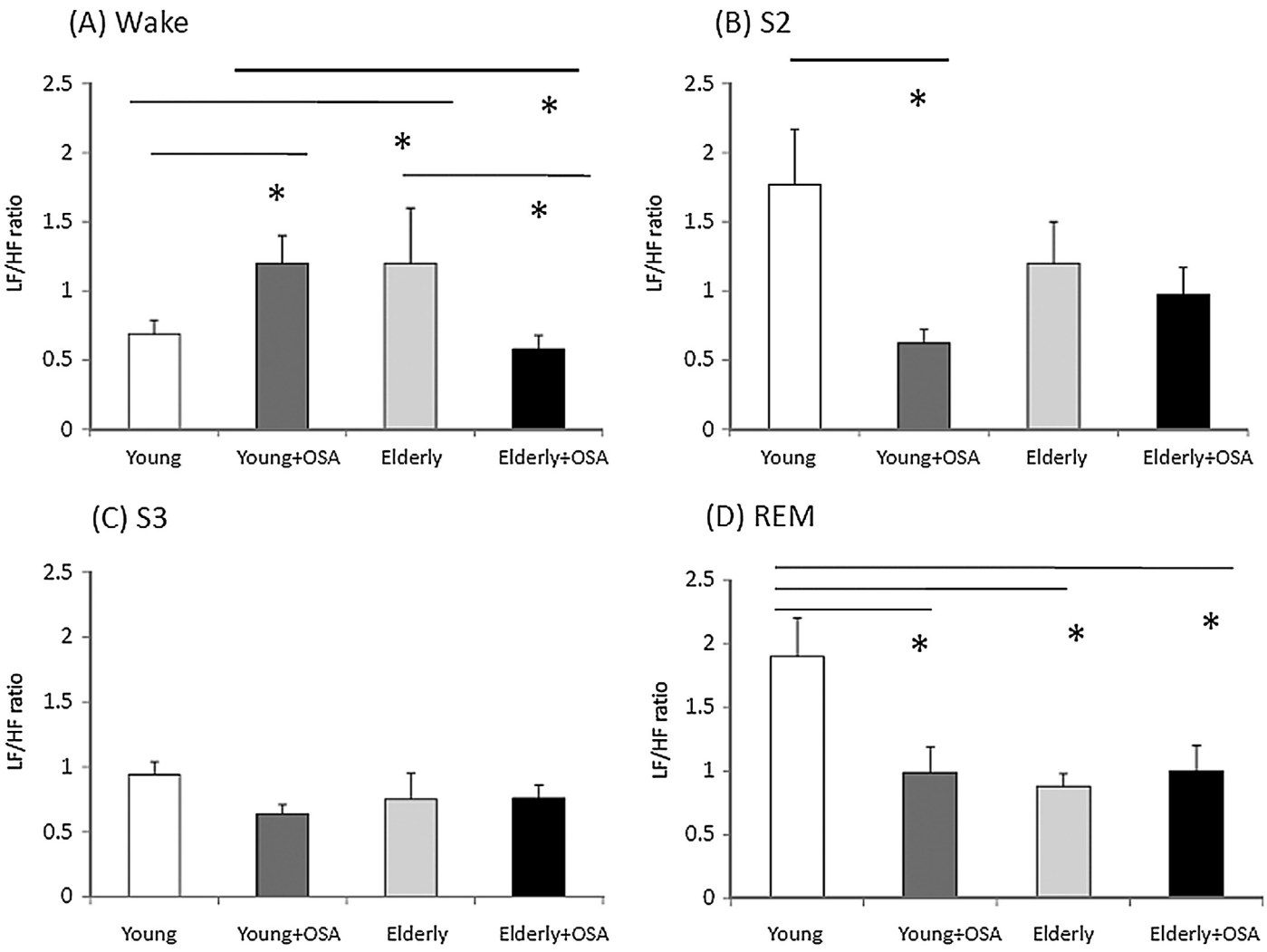

Fig. 3. Heart rate variability signal spectrum indices: low frequency/high frequency ratio during waking and different sleep stages. (A) Wake; (B) stage 2 (S2); (C) S3; (D) rapid eye movement (REM) sleep. $^{*}P < 0.05$.

The Sleep Heart Health Study [29] revealed gradual increases in the prevalence of sleep-disordered breathing with aging. Likewise, Ancoli-Israel et al. [30] found that 62% of individuals aged >60 years had AHI ≥ 10. The authors followed elderly residents in a community for 18 years to examine the natural history of sleep-disordered breathing. They observed that changes in severity of AHI were associated with changes in BMI, regardless of subject age.

Crasset et al. [31] compared HRV indices between young and elderly subjects without OSA during wakefulness and different sleep stages, and found that elderly subjects showed higher values of HR

Table 2
Heart rate variability indices during wakefulness and sleep of young and elderly.

Wake/sleep stage	Variable	Young ($n = 20$)	Young + OSA ($n = 30$)	Elderly ($n = 20$)	Elderly + OSA ($n = 30$)	*P*-value		
						Age effect	OSA effect	Interaction
Wake	LF/HF ratio	0.69 ± 0.1	1.2 ± 0.2	1.2 ± 0.4	0.53 ± 0.1	0.10	0.07	0.04
	LF	0.38 ± 0.04	0.46 ± 0.04	0.47 ± 0.06	0.33 ± 0.03	0.03	0.54	0.02
	HF	0.61 ± 0.04	0.53 ± 0.04	0.52 ± 0.06	0.66 ± 0.03	0.03	0.54	0.02
S2	LF/HF ratio	1.77 ± 0.4	0.62 ± 0.1	1.2 ± 0.3	0.97 ± 0.2	0.81	0.012	0.09
	LF	0.58 ± 0.04	0.36 ± 0.02	0.46 ± 0.04	0.40 ± 0.04	0.47	0.004	0.06
	HF	0.41 ± 0.04	0.64 ± 0.02	0.53 ± 0.04	0.59 ± 0.04	0.47	0.004	0.06
S3	LF/HF ratio	0.94 ± 0.1	0.64 ± 0.07	0.75 ± 0.2	0.76 ± 0.1	0.98	0.54	0.29
	LF	0.42 ± 0.40	0.37 ± 0.02	0.34 ± 0.04	0.36 ± 0.04	0.39	0.93	0.18
	HF	0.57 ± 0.04	0.62 ± 0.02	0.65 ± 0.04	0.63 ± 0.04	0.39	0.93	0.18
REM	LF/HF ratio	1.9 ± 0.3	0.99 ± 0.2	0.88 ± 0.1	1.0 ± 0.2	0.005	0.01	0.01
	LF	0.60 ± 0.04	0.42 ± 0.04	0.40 ± 0.04	0.42 ± 0.04	0.003	0.007	0.01
	HF	0.39 ± 0.04	0.57 ± 0.04	0.59 ± 0.04	0.57 ± 0.04	0.003	0.007	0.01

OSA, obstructive sleep apnea; LF/HF ratio, low frequency/high frequency ratio; LF, low frequency power; HF, high frequency power; S2, stage 2; S3, stage 3; REM, rapid eye movement sleep.

Table 3
Cardiorespiratory synchrony during wakefulness and sleep in young and elderly.

Wake/sleep stage	Variable	Young ($n = 20$)	Young + OSA ($n = 30$)	Elderly ($n = 20$)	Elderly + OSA ($n = 30$)	*P*		
						Age effect	OSA effect	Interaction
Wake	%TPCR	13.1 ± 2	11.8 ± 2	9.2 ± 1	6.7 ± 0.8	0.04	0.45	0.88
	%TPNCR	86.4 ± 3	88.1 ± 2	91.0 ± 1	92.9 ± 0.8	0.04	0.45	0.88
	Coherence HF	0.32 ± 0.07	0.23 ± 0.04	0.33 ± 0.06	0.29 ± 0.06	0.60	0.34	0.72
S2	%TPCR	10.1 ± 1	9.1 ± 1	12.1 ± 2	6.6 ± 1	0.82	0.009	0.07
	%TPNCR	89.8 ± 1	90.1 ± 1	87.8 ± 2	93.4 ± 1	0.82	0.009	0.07
	Coherence HF	0.40 ± 0.06	0.31 ± 0.03	0.46 ± 0.07	0.26 ± 0.05	0.94	0.046	0.42
S3	%TPCR	9.5 ± 1	9.8 ± 1	10.6 ± 1	9.1 ± 1	0.66	0.23	0.62
	%TPNCR	90.4 ± 0.9	90.1 ± 1	89.3 ± 1	90.9 ± 1	0.66	0.23	0.62
	Coherence HF	0.34 ± 0.06	0.29 ± 0.03	0.47 ± 0.08	0.40 ± 0.07	0.12	0.09	0.8
REM	%TPCR	8.9 ± 1	9.8 ± 1	9.0 ± 2	9.3 ± 1	0.88	0.66	0.83
	%TPNCR	91.0 ± 1	90.7 ± 1	90.9 ± 2	90.6 ± 1	0.88	0.66	0.83
	Coherence HF	0.32 ± 0.07	0.21 ± 0.03	0.36 ± 0.06	0.28 ± 0.04	0.55	0.17	0.86

OSA, obstructive sleep apnea; %TPCR, tachogram power coherent with respiration; %TPNCR, tachogram power not coherent with respiration; coherence HF, coherence between tachogram and respiration in high frequency band; S2, stage 2; S3, stage 3; REM, rapid eye movement.

and lower HF power during non-REM sleep compared with young subjects, suggesting that aging affects cardiac vagal activity during the night. They also observed that young individuals without OSA showed higher values of HF in non-REM sleep and that elderly subjects did not show the same behavior. In our study, we observed that elderly subjects presented with lower values for the LF/HF ratio and LF in S2 and REM sleep, which may be interpreted as a lower autonomic control during sleep in this population.

In another study [32] that analyzed HRV in healthy subjects without OSA during wakefulness, the authors observed lower HRV indices in elderly subjects during the day and at night. In our study, an interaction between age and OSA influenced the decrease in HRV during wakefulness, and this difference prevailed during REM sleep.

In a recent study, Viola et al. [33] applied nonlinear analysis of HRV during sleep in young and elderly subjects without OSA to characterize the complexity of signals by entropy measures. They observed that elderly subjects had lower levels of entropy during wakefulness and all stages of sleep, and this deficiency was most evident during REM sleep. They concluded that these changes are associated with a simplification of the mechanisms of cardiac control that could lead to a decreased ability of the cardiovascular system to respond to adverse cardiovascular events in elderly populations. In contrast, the current study only applied linear HRV analysis methods. The nonlinear analysis could be an interesting tool that is more sensitive to detecting changes when compared with traditional linear methods [21].

4.3. Contrasting the effect of OSA on HRV in young and elderly subjects

To compare the impact of OSA on autonomic control between young and elderly individuals, HRV indices were examined for these age-dependent groups with OSA. During sleep, the repeated episodes of OSA led to intermittent periods of hypoxia, hypercapnia with the activation and chemoreceptor reflexes, and to other mechanisms with a significant increase in sympathetic activation.

Notably, increased sympathetic activation is present even during wakefulness when subjects are breathing normally with no evidence of hypoxia or chemoreflex activation. The increase in HR and respiration in OSA may result in a decrease in cardiac vagal tone, increased cardiac sympathetic activation, or both [21]. In the current study, young OSA subjects had higher LF/HF ratio values during waking hours compared with young subjects, suggesting a higher sympathetic modulation in this group. Interestingly, there was a marked reduction of HRV indices in elderly patients with OSA during wakefulness. The LF/HF ratio was significantly reduced in old + OSA subjects. These results can be interpreted by a reduced cardiac modulation in elderly subjects, especially during wakefulness.

In several studies, the spectral analysis of HRV has been used to evaluate changes in autonomic function between stages of sleep [9,22,23,34], and the behavior of the LF/HF ratio during the different phases of sleep can provide physiological information to gain a better understanding of autonomic behavior in the presence of OSA.

In a previous study that used the same methodology as our study, healthy subjects without OSA demonstrated changes in HRV indices, with a decrease in the LF band during deep sleep and an increase during REM sleep. This suggests a decreased sympathetic modulation during deep sleep compared with wakefulness and increased sympathetic tone toward the end of each sleep cycle [24]. The expected change in sympathovagal balance during sleep, which markedly decreases during deep sleep and increases during REM sleep, was absent in young and elderly subjects with OSA [25].

Another study in subjects without OSA [34] found that a decreased LF/HF ratio was associated with synchronized sleep, which was accompanied by high HF values during the deeper stages of sleep, and a significant increase in the LF/HF ratio during REM. In subjects without OSA, the transition from wakefulness to light sleep is associated with a reduction in ventilation and HR; by contrast, during REM sleep, ventilation becomes highly variable and cardiovascular activity becomes irregular due to increased sympathetic nerve activity [22,34,35]. The behavior of HF power indicates increased vagal activity to the heart during deep sleep, which decreases during REM sleep.

When comparing the sleep stages between young and elderly subjects with OSA, a marked reduction was observed in HRV indices during sleep, in both groups. The LF/HF ratio was significantly reduced during S2 and REM sleep in young and elderly OSA groups, with an interaction between age and OSA in REM sleep. These results can be explained by an impaired cardiac autonomic modulation in both young and elderly patients with OSA, with a similar behavior in both groups. In a large cohort study, Song et al. [7] demonstrated how the HRV indices respond differently according to age and severity of OSA compared with individuals aged <60 years, observing that the LF/HF ratio is affected more by AHI than by age in this population.

4.4. Cardiorespiratory coupling in young and elderly subjects according to OSA

In order to determine whether the cardiorespiratory coupling in young and elderly subjects with and without OSA during

wakefulness and different stages of sleep is different, cardiorespiratory synchronization was compared in these groups. The HF band of HRV signal coincides with the respiratory rhythm, so the HF component may provide information on respiratory frequency and its modulation [36]. The phenomenon of HR fluctuations synchronized with breathing is a well-known phenomenon [i.e. respiratory sinus arrhythmia (RSA)] and consists of subtle rhythmic HR accelerations and decelerations synchronized to the respiratory cycle. There is clinical evidence that decreased RSA is a prognostic indicator for cardiac mortality [37].

The relationship between respiration and HR has been extensively studied over the years [34–37]. In a previous study using bivariate analysis, it was demonstrated that coherence between the tachogram and respirogram in the HF band increases progressively with synchronization of sleep and decreases REM sleep in healthy subjects [34,35]. In the current study, this same behavior was found in young people without OSA, with a marked decrease in %TPCR in elderly subjects during wakefulness. During sleep, the presence of OSA leads to a decrease in cardiorespiratory coupling during S2 in the OSA group.

These results may be explained by a lower synchronization between breathing and heartbeat during wakefulness, suggesting that aging leads to impaired cardiorespiratory synchronization, even during wakefulness, and that OSA has a negative impact on cardiorespiratory coordination during sleep. The cross-spectrum peak in the HF band being more pronounced and more narrowly distributed indicates a more regular breathing rhythm synchronized with cardiac activity, whereas the converse indicates a less pronounced synchronization between the respiratory and cardiac cycles [35].

Cardiorespiratory coordination may be affected during pathological conditions of sleep, as demonstrated in OSA patients [37]. In a large cohort study [37], which evaluated the cardiorespiratory coordination during sleep, the authors observed a significant reduction in cardiorespiratory coupling in severe OSA compared to those with mild OSA or without OSA. The authors suggested that cardiopulmonary synchronization is influenced by autonomic control that is affected by repetitive episodes of obstruction in OSA [37]. In our study, we could observe the same outcome in young subjects with OSA only in S2. However, the current study used different methods of analysis, as well as inclusion criteria with respect to mild, moderate, and severe OSA designations, both of which could have affected the consistency of previous and current findings. Additional studies are needed to investigate the mechanism involved in various degrees of severity of OSA in young and elderly patients and its possible clinical implications.

5. Conclusions

Our study reveals that the presence of OSA influenced HRV in young and elderly individuals, with reduced autonomic modulation during wakefulness and REM sleep. Age per se appeared to influence HRV during wakefulness and REM sleep in elderly subjects. Finally, the presence of OSA and age had an unfavorable impact on CRC during wakefulness and sleep. Thus, whereas OSA has negative effects on HRV and CRC across the lifespan, there seems to be an age-dependent influence with respect to how these negative effects manifest.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.05.028.

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